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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/938,763	08/27/2001	James Norman Cawse	rd-28,250	2912

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EXAMINER

LY, CHEYNE D

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 10/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/938,763	CAWSE, JAMES NORMAN	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7,9,10,13-36 and 39-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7,9,10,13-36 and 39-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u>10/03</u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants' arguments filed October 22, 2003 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
2. Claims 1-7, 9,10, 13-36, and 39-42 are examined on the merits.
3. Applicant argues that the final rejection mailed September 22, 2003 was improperly made. It is noted that Final Rejection status has been withdrawn. The instant Office Action is a NON-FINAL Office Action.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-7, 9, 10, 13-36, and 39-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
6. This rejection is maintained with respect to claims 1, 20, 35, and 36, as recited in the previous office action mailed September 22, 2003.

Response to Applicant's Arguments

7. Applicants' argument and pointed to support to overcome the above rejection as directed to claims 1, 20, 35, and 36 have been fully considered and found to be unpersuasive as discussed below.

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8. It is noted that the instant claims comprise the critical limitations "the positive interaction outside of the standard deviation to identify an effect." In order to succinctly point out the cause of said rejection the examiner has singled out the term "outside" in the previous rejections to emphasize it is this term alone which causes claims 1, 20, 35, and 36 claims to be vague and indefinite. Further, it has been acknowledged in the previous action that the phrase "standard deviation" is well known in the art. It is the use of the term "outside" in the claim limitation of "the positive interaction outside of the standard deviation to identify an effect" which causes the claims in their entirety vague and indefinite.

It is acknowledged that [0027] in the instant specification discloses "positive interactions can be identified outside of the deviation." However, Applicants do not set forth the criteria that are used to determine that specific identified effects are outside the standard deviation (greater or less than).

9. It is re-iterated that specific claims 1, lines 14 and 15; 10, (ii) and (ii); 20, line 2; 35, line 14; and 36, line 12, lines 14 and 15, the term "outside" causes the claim to be vague and indefinite because it is unclear as to what criteria are being used to determine that specific identified effects are outside the standard deviation (greater or less than). Clarification of the metes and bounds is required. Claims 2-7, 9, 10, 13-34 and 39-42 are rejected for being directly or indirectly dependent from claim 1, 35, or 36.

10. Specific to claim 10, (iii), the variable at the end of line 1 is vague and indefinite because it is unclear what the symbol represents? Clarification of the metes and bounds is required.

LACK OF ENABLEMENT UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for defining leads from a complex chemical space (page 11-18), does not reasonably provide enablement for defining leads for a commercial process. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

13. This rejection is maintained with respect to claim 16, as recited in the previous office action mailed September 22, 2003.

14. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that

although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

Response to Applicant's Arguments

15. Applicant argues, "claim 16 does not claim a commercial process; claim 16 claims a process that identifies a "best set of factor levels [that define] leads for a commercial process." Applicants' argument have been fully considered and found to be unpersuasive because the scope of the instant claim 16 includes the critical limitation of a commercial process.

It is acknowledged that the claim limitation of "commercial process" further limits the factor levels that define leads. However, it is the recitation of such further limitation in claim 16, which determines the claimed subject matter of said claim. The embodiment of the claimed invention as directed to claims 16 is determined by the all the limitations of said claim.

Therefore, the instant specification as originally filed does not provide enablement support as commensurate in scope with said claim as determined be the recited limitations.

16. It is re-iterated the instant "invention provides a particularly well-suited experimental methodology to investigate multiple and complex interactions of a catalyzed chemical reaction" (page 3, lines 13-20). However, the instant application does not provide guidance or working examples for translating an experimental methodology for generating leads to a generic commercial process for using the said leads. It is well established that experimental methods require many iterations of trial and errors processes to refine an experimental process to a commercial process. Therefore, The instant specification does not provide

sufficient guidance or working examples for one skilled in the art to predictably use the claimed invention for a commercial process.

CLAIM REJECTIONS - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

18. Claims 1-7, 9, 10, 13-28, 34-36, and 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrafiotis et al. (US 5,901,069 A) taken with Grate et al. (US 6,408,250 B1).

19. This rejection is maintained with respect to claims 1-7, 9, 10, 13-28, 34-36, and 39-42, as recited in the previous office action mailed September 22, 2003.

Response to Applicant's Arguments

20. Applicant argues that Agrafiotis et al., Grate et al., and Chaudhari et al. references are not properly combinable for a number reasons. First, Agrafiotis et al. and Grate do not teach or suggest that any method for "generation of chemical entities" is applicable to a "classifying and identifying" method. Second, there is no motivation to improve the Agrafiotis et al. method for "generation of chemical entities" by a "classifying and identifying" as taught by Grate et al. Further, the PTO has failed to provide any "logical and rational" reasoning to combine the disclosures of the above references with Chaudhari et al.

21. Applicant's argument has been fully considered and found to be unpersuasive.

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22. Agrafiotis et al. discloses a system and method for efficiently and effectively generating new leads (identifying) (column 3, lines 27-29) with improved activity and properties (column 4, lines 7-12) by analyzing the leads compounds to identify which of said compounds were adequately synthesized, and which of the compounds were not adequately synthesized based on chemical data (classification) (column 6, lines 2-20). The improvement disclosed by Agrafiotis et al. as cited above provides sufficient motivation to one of ordinary skill to improve on said method by using a matrix algebra for characterizing, classifying, and identifying chemicals in a sample as taught by Grate et al. (Column 14, equation 10).

Further, the said disclosure of Agrafiotis et al. sufficiently motivates of one of ordinary skill to improve on the said method of Agrafiotis et al. and Grate et al. for using a matrix algebra to characterize, classify, and identify chemicals in a sample using a palladium, halide or co-catalysts as taught by Chaudhari et al.

23. Therefore, the above cited motivation to combine references Agrafiotis et al., Grate et al., and Chaudhari et al. provides an adequate prima case of obviousness to a person of ordinary skill in the art that the teachings of Agrafiotis et al., Grate et al., and Chaudhari et al. in combination suggests the instant claimed subject matter.

24. It is re-iterated that Agrafiotis et al. discloses a method of defining an experimental space such as a combinatorial chemical library where a combinatorial chemical library could be constructed from chemical building blocks designated as A, B, and C. Further, the compounds in the combinatorial chemical library are equal to two in length, then, the

compounds would be generated are: AA, AB,...and CC (total of nine) (column 5, lines 5-18), as in instant claims 2, 3, and 5-7.

25. Agrafiotis et al. discloses said method comprising a linear model (column 17, lines 47-52), as in instant claim 4.

26. The chemical building blocks comprise of 100 commercially available agents (column 5, lines 37-40), as in instant claim 16.

27. The system may perform tests and evaluations on one or more structure-activity models in parallel (column 6, lines 43-45), as in instant claim 23. The method of Agrafiotis et al. performs selective micro scale solid-state synthesis of a specific combinatorial library of directed diversity library (column 8, lines 43-45), as in instant claim 24.

28. The lead generation/optimization system is implemented in an iterative process wherein instructions are sent to a robotic synthesis system and reagents are mixed compounds are synthesized. The said compounds are assayed and ranked; the best-ranked compound is selected (§ Operation of the present invention, columns 13-21) as in instant claims 15, 17, 25-28, and 34.

29. The system of Agrafiotis et al. comprises a processor and controller (Figure 1) wherein the reactions occur defined space of 96 well plates (column 20, lines 51-67), and a detection device (column 10, lines 5-14), as in instant claims 39-42.

30. However, Agrafiotis et al. does not disclose the method of defining experimental space wherein the analysis is done according the steps defined in claims 1, 35 and 36 of this instant application.

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31. Grate et al. discloses the use of matrix algebra for characterizing, classifying, and identifying unknowns in a sample (Column 14, equation 10). Grate et al. defines matrices P containing the coefficients that are related to a plurality of descriptors (column 6, lines 59-65), as in claim 1, step (A).

32. Matrix R where $R = C^{-1}(VP + I)^{-1}N$ (column 7, lines 7 and 8), as in claim 1, step (B) and claim 9. P^T is the transpose of matrix P (column 7, lines 16-17 and equations 12-14), as in claim 1, step (C) and claim 10, steps (ii) and (iii).

33. The concentrations are plotted versus the fraction noise (RMSEP) in the data (e.g. 0.1 indicates that the standard deviation of the noise was 10% of the sensor signal) (column 20, lines 35-40 and Figure 1), as in claim 1, steps (i), (ii), and (iii); and claims 35 and 36.

34. The inclusion of a document from Dictionray.com is not intended to be used as prior but only to expand on the standard deviation disclosure of Grate et al. Dictionary.com discloses that it is well know in the art that the calculation of standard deviation is derived from a random variable (page 2, line 10).

35. Further, Grate et al. discloses equations 15-20 (column 15, lines 5-33) in an inverse least approach for descriptor y, as in instant claims 18-22.

36. It is noted that Agrafiotis et al. discloses an improvement for a general system and method for efficiently and effectively generating of chemical entities with defined physical, chemical or bioactive properties for drug lead identification via a chemical library (column 1, lines 15-23 and column 3, lines 27-29). The suggested improvement of Agrafiotis et al. is directly applicable to generation of chemical for the characterization, classifying, and identifying as taught by Grate et al.

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37. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the concept emphasized by Agrafiotis et al. for an iterative process for generating chemical entities with define physical properties and/or bioactive properties (Abstract etc.) and improve on it by utilizing the method of Grate et al. which comprises using the properties chemical entities to identify a chemical sample. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the method of Agrafiotis et al. for generating chemical entities and determining the properties directed to the chemical entities; and identify and characterize the said chemical entities according to the method of Grate et al. which comprises an algebra matrix for identifying a sample.

38. Claims 1-7, 9, 10, 13-36, and 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrafiotis et al. (US 5,901,069 A) taken with Grate et al. (US 6,408,250 B1) in view of Chaudhari et al. (US 5,917,077 A).

39. This rejection is maintained with respect to claims 1-7, 9, 10, 13-36, and 39-42, as recited in the previous office action office action mailed September 22, 2003.

40. Agrafiotis et al. discloses a method of defining an experimental space such as a combinatorial chemical library. Further, Grate et al. discloses the use of matrix algebra for characterizing, classifying, and identifying unknowns in a sample (Column 14, equation 10) as directed claims 1-7, 9, 10, 13-28, 34-36, and 39-42 cited above.

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41. However, Agrafiotis et al. taken with Grate et al. does not disclose the limitation of palladium, halide or co-catalysts, which are the embodiments of the above listed instant claim rejected hereunder.

42. Chaudhari et al. discloses a method for preparing chemical entities using catalyst such as the metals of Group IIIB such as palladium and halide (Abstract etc.). Further, the method of Chaudhari et al. includes inorganic co-catalysts (column 1, lines 33-34), as in instant claims 29-33.

43. It is noted that Agrafiotis et al. discloses an improvement for a general system and method for efficiently and effectively generating of chemical entities with defined physical, chemical or bioactive properties for drug lead identification via a chemical library (column 1, lines 15-23 and column 3, lines 27-29). The suggested improvement of Agrafiotis et al. is directly applicable to generation of chemical for the characterization, classifying, and identifying as taught by Grate et al. and Chaudhari et al.

44. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the concept emphasized by Agrafiotis et al. for an iterative process for generating chemical entities with define physical properties and/or bioactive properties (Abstract etc.) and improve on it by utilizing the method of Grate et al. which comprises using the properties chemical entities to identify a chemical sample such as catalysts (palladium and halide composition) and inorganic catalysts as taught by Chaudhari et al.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the method of Agrafiotis et al. for generating chemical entities and determining the properties as directed to the said chemical entities; and characterize the

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said chemical entities according to the method of Grate et al. using an algebra matrix and improve on the methods of Agrafiotis et al. and Grate et al. by including such chemical entities as catalysts (palladium and halide composition) and inorganic catalysts as taught by Chaudhari et al.

CONCLUSION

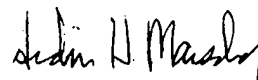
45. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

46. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

47. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

48. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
10/28/03


ARDIN H. MARSCHEL
LEGAL INSTRUMENTS EXAMINER